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(54) Title: 3'-PRODRUGS OF 2'-DEOXY-β-L-NUCLEOSIDES

(57) Abstract: The present invention relates to compounds, compositions and methods for the treatment of a host infected with a hepatitis B virus. Specifically, compounds and compositions of 3'-esters of 2'-deoxy-β-L-nucleosides are disclosed, which can be administered either alone or in combination with other anti-hepatitis B agents. Compounds and compositions of 3',5'-esters of 2'-deoxy-β-L-nucleosides are disclosed, which can be administered either alone or in combination with other anti-hepatitis B agents, are also disclosed.



### INTERNATIONAL SEARCH REPORT

Intel onal Application No PCT/US 01/19147

A. CLASSI IPC 7	FICATION OF SUBJECT MATTER C07H19/06 C07H19/16 A61K31/	7068 A61P31/12								
According to International Patent Classification (IPC) or to both national classification and IPC										
B. FIELDS	SEARCHED									
Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07H A61K A61P										
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched										
	ata base consulted during the international search (name of data ba ternal, WPI Data, CHEM ABS Data	se and, where practical, search terms used								
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT									
Category *	Citation of document, with indication, where appropriate, of the re-	levant passages	Relevant to claim No.							
X	WO 00 09531 A (NOVIRIO PHARMACEUT LIMITE; IMBACH JEAN LOUIS; GOSSEIGILLES) 24 February 2000 (2000-02 cited in the application the whole document	1-194								
х	V. SKARIC ET AL.: "Aminoacyl der of 4-thiothymidine, cytosine and CROATICA CHEMICA ACTA, vol. 48, no. 3, 1976, pages 351-3 XP001034973 page 352	1-4,6-8								
	·	-/	٠.							
X Furth	ner documents are listed in the continuation of box C.	X Patent family members are listed	in annex.							
*A* document defining the general state of the art which is not considered to be of particular relevance  *E* earlier document but published on or after the international filling date  *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  *O* document referring to an oral disclosure, use, exhibition or other means  *P* document published prior to the international filling date but		"Y" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  "&" document member of the same patent family  Date of mailing of the international search report								
	8 November 2001	21/02/2002								
Name and n	nailing address of the ISA  European Patent Office, P.B. 5818 Patentiaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo nt, Fax (+31-70) 340-3016	Authorized officer  de Nooy, A								

### INTERNATIONAL SEARCH REPORT

Inter Snal Application No
PCT/US 01/19147

		FC1/US U1/1914/
C.(Continu	etion) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	ation of document, with indication, where appropriate, of the relevant passages  Relevant to claim No	
X	WANG P ET AL: "RECENT ADVANCES IN L-NUCLEOSIDES: CHEMISTRY AND BIOLOGY" ANTIVIRAL RESEARCH, ELSEVIER SCIENCE BV., AMSTERDAM, NL, vol. 46, no. 1/2, 1998, pages 19-44, XP000944025 ISSN: 0166-3542 scheme 2 conclusions	1,156
X	US 5 559 101 A (WEIS ALEXANDER L ET AL) 24 September 1996 (1996-09-24) the whole document	1,2
X	WO 92 08727 A (CONSIGLIO NAZIONALE RICERCHE ;MENARINI RICERCHE SUD SPA (IT)) 29 May 1992 (1992-05-29) the whole document	1,2
X	BOUDOU V ET AL: "A new and convenient approach for the synthesis of ribo- and 2'-deoxyribo-beta-L-furanonucleosides starting from beta-L-xylofuranonucleosides" NUCLEOSIDES & NUCLEOTIDES, MARCEL DEKKER, INC, US, vol. 18, no. 45, 1999, pages 607-609, XP002164642 ISSN: 0732-8311 the whole document	1,156
A	RYU E K ET AL: "AMINOACYL DERIVATIVES OF NUCLEOSIDES, NUCLEOTIDES, AND POLYNUCLEOTIDES. XXVII GENERAL SYNTHESIS OF 2'(3')-O-AMINOACYL DINUCLEOSIDE PHOSPHATES DERIVED FROM THE AA-TRNA TERMINUS"  JOURNAL OF CARBOHYDRATES. NUCLEOSIDES NUCLEOTIDES, MARCEL DEKKER, BASEL, CH, vol. 4, no. 6, 1977, pages 387-408, XP000564974 ISSN: 0094-0585 structures 4b-e	4

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### INTERNATIONAL SEARCH REPORT

information on patent family members

Inter. onal Application No PCT/US 01/19147

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 0009531	A	24-02-2000	AU CN EP WO	5475799 A 1320128 T 1104436 A2 0009531 A2	06-03-2000 31-10-2001 06-06-2001 24-02-2000
US 5559101	A	24-09-1996	EP JP WO	0788506 A2 10507772 T 9613512 A2	13-08-1997 28-07-1998 09-05-1996
WO 9208727	Α	29-05-1992	IT AU WO	1246983 B 8923291 A 9208727 A1	12-12-1994 11-06-1992 29-05-1992